MEDICAL INFORMATION

April 7, 2016

Dear Dave Campana:

Thank you for your inquiry about QUILLICHEW ER C-II (methylphenidate HCl extended-release chewable tablet).

Enclosed you will find a PDF copy of the Brief Product Summary and a relevant pharmacokinetic reference for QuilliChew ER. QuilliChew ER will be reviewed on April 27th, 2016 by the Montana DUR committee. All pharmacoeconomic references were removed as per the guidance on your website. Please keep in mind that this information was prepared with the understanding that it should not be disclosed to anyone other than those who in the course of their job responsibilities require access to the Brief Product Summary.

If you did not specifically request this information, please call 1-800-438-1985 to report this to us.

I hope the information enclosed proves to be of help and interest. Please do not hesitate to contact us at 1-800-438-1985, or via www.pfizermedinfo.com, should you require anything further.

Sincerely,

Chris Gutteridge, PharmD.
Pfizer Medical Information

US16-020835

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This information is supplied as a professional courtesy in response to your inquiry. It is intended to provide pertinent data to assist you in forming your own conclusions and making decisions. The information is not intended to advocate any indication, dosage or other claim that is not covered in the product prescribing information, which can be accessed on www.pfizer.com or by contacting us.

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QuilliChew ER, C-II – Montana Brief Product Summary

QuilliChew ER™ (methylphenidate HCl) extended-release chewable tablets, for oral use, CII
BRIEF PRODUCT SUMMARY

The purpose of this document is to provide the clinical and/or pharmacoeconomic information regarding QuilliChew ER that was requested; it is not intended to be used for any other purpose. This document contains relevant information for QuilliChew ER, which may or may not be included in the US Prescribing Information (USPI). Pfizer does not suggest or recommend the use of QuilliChew ER in any manner other than as described in the USPI.

CLINICAL BACKGROUND, BURDEN OF ILLNESS AND TREATMENT: Attention-Deficit/Hyperactivity Disorder (ADHD) is characterized by a persistent and developmentally inappropriate pattern of inattention, hyperactivity and/or impulsivity.[1] ADHD has a lifetime prevalence of approximately 9.5% of children and adolescents[2,3] and 4.4% of adults[2] in the US. Core symptoms observed during childhood usually persist into adulthood and cause impairment across multiple domains (e.g., school, work, family).[4] Particularly when untreated, ADHD is associated with increased risk for pedestrian, bicycle and vehicular accidents; antisocial behavior and criminality; nicotine dependence and substance abuse; family and social problems; and poor academic and occupational achievement.[4,5,6,7,8] Clinical practice guidelines have long supported ADHD treatment in children and adolescents, which may include a Food and Drug Administration (FDA)-approved stimulant.[9,10]

PRODUCT VALUE: QuilliChew ER is intended to address the unmet need for an oral extended-release (ER) stimulant formulation that can be taken by patients who have problems swallowing pills. Other ER stimulant tablet and capsule formulations cannot be crushed. Those that can be sprinkled on applesauce[11,12,13,14] or dissolved in water[15] may be cumbersome to administer, rejected by patients who find that food does not mask the unpleasant taste or texture, and not completely consumed (thereby potentially resulting in exposure to less than the full prescribed dose). In addition, children and adolescents who have problems in adhering to oral formulations (including oral suspensions and pills) may find QuilliChew ER to be palatable and more appealing.

QuilliChew ER is the first once-daily, ER chewable tablet methylphenidate (MPH) formulation approved for the treatment of ADHD.[16] Cherry-flavored, this formulation contains approximately 30% immediate-release (IR) and 70% ER MPH.[16]

INDICATIONS AND USAGE: QuilliChew ER is a central nervous system (CNS) stimulant indicated for the treatment of ADHD.[16] The efficacy of QuilliChew ER was evaluated in a double-blind, randomized, placebo-controlled, laboratory classroom, parallel group study in 90 children (aged 6 to 12 years) who met Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV®) criteria for ADHD. QuilliChew ER is available as 20 mg, 30 mg and 40 mg ER chewable tablets for oral administration. The 20 mg and 30 mg extended-release chewable tablets are scored and may be divided into equal halves for dose adjustments. Assess for the presence of cardiac disease (i.e. perform a careful history, family history of sudden death or ventricular arrhythmia and physical exam) before prescribing QuilliChew ER. The recommended starting dose of QuilliChew ER for patients 6 years and above is 20 mg once daily orally in the morning. The dose may be titrated weekly by 10 mg, 15 mg, or 20 mg. The dose should be individualized according to the needs and responses of the patient. Daily doses above 60 mg have not been studied and are not recommended. Healthcare providers should periodically re-evaluate any long-term use of QuilliChew ER, and adjust dosage as needed.[16]

PHARMACOKINETICS: Following a single oral dose of 40 mg QuilliChew ER in 31 healthy adult subjects in a crossover study under fasting conditions, MPH mean (± SD) peak plasma concentration of 12.5 (±3.68) ng/mL occurred at a median time of 5.0 hours after dosing. Compared to an IR formulation of MPH chewable tablet (40 mg in 2 equal doses of 20 mg, 6 hours apart), MPH mean

peak concentration and exposure (AUC_{inf}) was about 20% and 11% lower, respectively, after single dose administration of 40 mg QuilliChew ER.[16,17]

CLINICAL EFFICACY AND SAFETY: The efficacy and safety of QuilliChew ER was evaluated in a double-blind, randomized, placebo-controlled, laboratory classroom, parallel group study in 90 children ages 6 to 12 years with a diagnosis of ADHD. Subjects completed a 6-week open-label dose optimization period followed by a 1-week, double-blind, crossover treatment of the individually optimized dose of QuilliChew ER (20-60 mg/day) or placebo. The intent-to-treat (ITT) population consisted of 85 randomized subjects who received at least 1 dose of double-blind study drug and had at least 1 post-baseline assessment of the primary efficacy variable. At the end of the double-blind treatment phase, trained observers evaluated the attention and behavior of subjects in a laboratory classroom using the Swanson, Kotkin, Agler, M-Flynn and Pelham (SKAMP) rating scale.[16] Among the 85 ITT population, the average of all post-dose SKAMP-Combined scores at the end of the treatment period (the primary efficacy endpoint) was statistically significantly lower (improved) with QuilliChew ER compared to placebo [$p<0.001$; Least Squares means (standard errors) were 12.1(1.41) for QuilliChew ER and 19.1(1.39) for the placebo]. The results from this study demonstrated statistically significant improvements in attention and behavior in subjects treated with QuilliChew ER versus placebo.[16,18]

QuilliChew ER has a high potential for abuse and dependence and may be associated with serious cardiovascular reactions, blood pressure and heart rate increases, psychiatric adverse reactions, priapism, peripheral vasculopathy, long-term suppression of growth, and risks in phenylketonurics.[16]

Please refer to the QuilliChew ER full Prescribing Information including Boxed Warning for additional information on Contraindications, Warnings, Precautions, Pharmacokinetics, and Adverse Events. Approved full Prescribing Information including Boxed Warning on QuilliChew ER can be accessed at https://www.pfizermedicalinformation.com/en-us/quillichew-er.Alternatively, the product's approved prescribing information may be accessed at www.pfizer.com.

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